

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P102159WO/SW	FOR FURTHER ACTION		see Form PCT/ISA/220 as well as, where applicable, Item 5 below.
International application No. PCT/GB2004/001128	International filing date (day/month/year) 17/03/2004	(Earliest) Priority Date (day/month/year) 18/03/2003	
Applicant MILNER, JO			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.

The International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, see Box No. I.

2. Certain claims were found unsearchable (See Box II).

3. Unity of invention is lacking (see Box III).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. 1

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b. none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

Int'l Application No	PCT/EP2004/001128
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A. CLASSIFICATION OF SUBJECT MATTER		
IPC 7 C07K14/47 C12N15/11 A61K48/00 A61P35/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K C12N A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, WPI Data, PAJ		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CIOCA DANIEL P ET AL: "RNA interference is a functional pathway with therapeutic potential in human myeloid leukemia cell lines." CANCER GENE THERAPY, vol. 10, no. 2, February 2003 (2003-02), pages 125-133, XP002293680 ISSN: 0929-1903 page 126, left-hand column, last paragraph - right-hand column, paragraph 1 figures 1,3 Y page 132, left-hand column, paragraph 3 ----- -/-	1-4, 7-11, 15-18 19
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		<input checked="" type="checkbox"/> Patent family members are listed in annex.
* Special categories of cited documents :		
'A' document defining the general state of the art which is not considered to be of particular relevance		'T' later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
'E' earlier document but published on or after the International filing date		'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
'L' document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
'O' document referring to an oral disclosure, use, exhibition or other means		
'P' document published prior to the International filing date but later than the priority date claimed		'S' document member of the same patent family
Date of the actual completion of the International search	Date of mailing of the International search report	
26 October 2004	08.11.2004	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl Fax: (+31-70) 340-3016	Authorized officer ALCONADA RODRIGUEZ	

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Int. Search Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FUTAMI TAKASHI ET AL: "Induction of apoptosis in HeLa cells with siRNA expression vector targeted against bcl-2." NUCLEIC ACIDS RESEARCH. SUPPLEMENT (2001) 2002, no. 2, 2002, pages 251-252, XP002264267 abstract	1-4, 7-11, 15-20
Y	-----	19
X	WO 02/055692 A (VORNLOCHER HANS-PETER ; LIMMER STEFAN (DE); RIBOPHARMA AG (DE); GEICK) 18 July 2002 (2002-07-18) page 5, lines 17-26 page 7, lines 18-22 page 3, lines 19-33 page 6, lines 10-26	1,2, 5-10,13, 15-18
Y	GAUTSCHI O ET AL: "ACTIVITY OF A NOVEL BCL-2/BCL-XL-BISPECIFIC ANTISENSE OLIGONUCLEOTIDE AGAINST TUMORS OF DIVERSE HISTOLOGIC ORIGINS" JOURNAL OF THE NATIONAL CANCER INSTITUTE, US DEPT. OF HEALTH, EDUCATION AND WELFARE, PUBLIC HEALTH, US, vol. 93, no. 6, 21 March 2001 (2001-03-21), pages 463-471, XP009003270 ISSN: 0027-8874 figures 2-4	19
A	US 6 414 134 B1 (REED JOHN C) 2 July 2002 (2002-07-02) the whole document	
P,X	WO 03/070969 A (MC SWIGGEN JAMES ; BEIGELMAN LEONID (US); SIRNA THERAPEUTICS INC (US)) 28 August 2003 (2003-08-28) page 7, lines 17-20; examples 4-10; tables II, III	1-5, 7-11,13, 15-20
P,X	WACHECK VOLKER ET AL: "Small interfering RNA targeting Bcl-2 sensitizes malignant melanoma." OLIGONUCLEOTIDES, vol. 13, no. 5, October 2003 (2003-10), pages 393-400, XP001189796 ISSN: 1545-4576 page 394, right-hand column, paragraph 2; figures 4,5	1-4, 7-11, 15-18
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C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	JIANG MING ET AL: "Bcl-2 constitutively suppresses p53-dependent apoptosis in colorectal cancer cells." GENES AND DEVELOPMENT, vol. 17, no. 7, 1 April 2003 (2003-04-01), pages 832-837, XP002293683 ISSN: 0890-9369 the whole document	1-4, 7-12, 15-20
P,X	CAO XIAOBO X ET AL: "A short-interfering RNA (siRNA) duplex targeted to BCL-XL significantly reduces BCL-XL expression and enhances response to chemotherapy in mesothelioma." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 44, July 2003 (2003-07), page 1098, XP001182915 & 94TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, WASHINGTON, DC, USA; JULY 11-14, 2003 ISSN: 0197-016X abstract	1,2, 5-10, 13-20
P,X	ZENDER L ET AL: "Small interfering RNA (siRNA) and antisense oligonucleotides (ASO) for reversion of chemotherapy resistance in hepatoma cells." JOURNAL OF HEPATOLOGY, vol. 38, no. Supplement 2, April 2003 (2003-04), page 107, XP002301756 & 38TH ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER, INSTANBUL, TURKEY; MARCH 29-APRIL 01, 2003 ISSN: 0168-8278 abstract	1,2, 5-10,13, 15-18
P,X	WALTEMATHE M ET AL: "Essential role for bcl-xL as an antiapoptotic factor in TRAIL mediated apoptosis of hepatocytes during viral infection." JOURNAL OF HEPATOLOGY, vol. 38, no. Supplement 2, April 2003 (2003-04), page 107, XP002301757 & 38TH ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER, INSTANBUL, TURKEY; MARCH 29-APRIL 01, 2003 ISSN: 0168-8278 abstract	1,2, 5-10,13, 15-18
P,X	WO 03/040366 A (HAREL-BELLAN ANNICK ; DAUTRY FRANCOIS (FR); AIT-SI-ALI SLIMANE (FR); C) 15 May 2003 (2003-05-15) claims 14,15,28,31	1,2,5, 7-10,13, 15-18

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material
 - in written format
 - in computer readable form
 - c. time of filing/furnishing
 - contained in the international application as filed
 - filed together with the international application in computer readable form
 - furnished subsequently to this Authority for the purpose of search
2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-7, as far as relating to an *in vivo* method, and claims 15 and 16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,2,7-10, 15-20 (in part) and 3, 4,11, 12 (complete)

A siRNA construct which is homologous to the Bcl-2 mRNA; method of regulating apoptosis and of treating diseases associated with inappropriate apoptosis by introducing said siRNA into a cell.

2. claims: 1,2,7-10, 15-20 (in part) and 5, 6, 13, 14 (complete)

As invention 1 but relating to an siRNA construct which is homologous to the Bcl-XL mRNA.

INTERNATIONAL SEARCH REPORT

b. International Application No
... JB2004/001128

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 02055692	A	18-07-2002		DE 10100586 C1 CA 2432341 A1 CA 2432350 A1 WO 02055692 A2 WO 02055693 A2 EP 1349927 A2 EP 1352061 A2 ES 2204360 T1 JP 2004519457 T JP 2004519458 T US 2004001811 A1 US 2004175703 A1 ZA 200304500 A	11-04-2002 18-07-2002 18-07-2002 18-07-2002 18-07-2002 08-10-2003 15-10-2003 01-05-2004 02-07-2004 02-07-2004 01-01-2004 09-09-2004 18-11-2003
US 6414134	B1	02-07-2002		US 6040181 A US 5831066 A CA 2172153 A1 EP 0722342 A1 JP 2001505401 T JP 2003026609 A WO 9508350 A1 US 5734033 A	21-03-2000 03-11-1998 30-03-1995 24-07-1996 24-04-2001 29-01-2003 30-03-1995 31-03-1998
WO 03070969	A	28-08-2003		CA 2455447 A1 CA 2455506 A1 CA 2456444 A1 CA 2457528 A1 CA 2459532 A1 CA 2463595 A1 CA 2471421 A1 CA 2476112 A1 EP 1432724 A1 EP 1463842 A1 EP 1465910 A2 EP 1423404 A2 EP 1442143 A2 EP 1448590 A2 EP 1432725 A1 EP 1448580 A2 EP 1430157 A2 EP 1458741 A2 EP 1436314 A2 EP 1423406 A2 GB 2396864 A GB 2396155 A GB 2396616 A GB 2397062 A GB 2397818 A WO 03072590 A1 WO 03072704 A2 WO 03072705 A2 WO 03070983 A1 WO 03070742 A1 WO 03070881 A2 WO 03070884 A2 WO 03070885 A2 WO 03070886 A2 WO 03070743 A1	12-09-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003 30-06-2004 06-10-2004 13-10-2004 02-06-2004 04-08-2004 25-08-2004 30-06-2004 25-08-2004 23-06-2004 22-09-2004 14-07-2004 02-06-2004 07-07-2004 16-06-2004 30-06-2004 14-07-2004 04-08-2004 04-09-2003 04-09-2003 04-09-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003 28-08-2003

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Int'l. Appl. No.
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Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 03070969	A		WO 03070887 A2	28-08-2003
			WO 03070888 A2	28-08-2003
			WO 03070966 A2	28-08-2003
			WO 03070744 A1	28-08-2003
WO 03040366	A	15-05-2003	FR 2832154 A1	16-05-2003
			FR 2838442 A1	17-10-2003
			CA 2466773 A1	15-05-2003
			EP 1453962 A2	08-09-2004
			WO 03040366 A2	15-05-2003